

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number  
**WO 2005/061463 A1**

(51) International Patent Classification<sup>7</sup>: C07D 231/12,  
413/10, 401/10, A61K 31/415, A61P 37/02

(21) International Application Number:  
PCT/GB2004/005464

(22) International Filing Date:  
23 December 2004 (23.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0329617.5 23 December 2003 (23.12.2003) GB  
60/532,199 23 December 2003 (23.12.2003) US  
60/577,843 8 June 2004 (08.06.2004) US

(71) Applicants (for all designated States except US): ASTEX  
TECHNOLOGY LIMITED [GB/GB]; 436 Cambridge  
Science Park, Milton Road, Cambridge CB4 0QA (GB).  
CANCER RESEARCH TECHNOLOGY LIMITED  
[GB/GB]; Sardinia House, Sardinia Street, London WC2A  
3NL (GB). THE INSTITUTE OF CANCER RE-  
SEARCH: ROYAL CANCER HOSPITAL [GB/GB];  
123 Old Brompton Road, London SW7 3RP (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BERDINI, Valerio  
[IT/GB]; 436 Cambridge Science Park, Milton Road, Cam-  
bridge CB4 0QA (GB). SAXTY, Gordon [GB/GB]; 436  
Cambridge Science Park, Milton Road, Cambridge CB4  
0QA (GB). VERDONK, Marinus, Leendert [NL/GB];  
436 Cambridge Science Park, Milton Road, Cambridge

CB4 0QA (GB). WOODHEAD, Steven, John [GB/GB];  
436 Cambridge Science Park, Milton Road, Cambridge  
CB4 0QA (GB). WYATT, Paul, Graham [GB/GB];  
436 Cambridge Science Park, Milton Road, Cambridge  
CB4 0QA (GB). BOYLE, Robert, George [GB/GB];  
436 Cambridge Science Park, Milton Road, Cambridge  
CB4 0QA (GB). SORE, Hannah, Fiona [GB/GB]; 436  
Cambridge Science Park, Milton Road, Cambridge CB4  
0QA (GB). WALKER, David, Winter [GB/GB]; 436  
Cambridge Science Park, Milton Road, Cambridge CB4  
0QA (GB). COLLINS, Ian [GB/GB]; Cancer Research  
UK, 15 Cotswold Road, Sutton SM2 5NG (GB). DOWN-  
HAM, Robert [GB/GB]; 436 Cambridge Science Park,  
Milton Road, Cambridge CB4 0QA (GB). CARR, Robin,  
Arthur, Ellis [GB/GB]; 436 Cambridge Science Park,  
Milton Road, Cambridge CB4 0QA (GB).

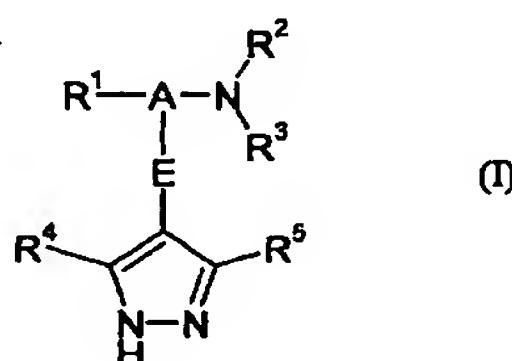
(74) Agent: HUTCHINS, Michael, Richard; M.R. Hutchins  
& Co., 23 Mount Sion, Tunbridge Wells, Kent TN1 1TZ  
(GB).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: PYRAZOLE DERIVATIVES AS PROTEIN KINASE MODULATORS



(57) Abstract: The invention provides compounds of the formula: (I) having protein kinase B inhibiting activity: wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup> and a maximum chain length of 4 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom a with respect to the NR<sup>2</sup>R<sup>3</sup> group and provided that the oxo group when present is located at a carbon atom a with respect to the NR<sup>2</sup>R<sup>3</sup> group; E is a monocyclic or bicyclic carbocyclic or heterocyclic group; R<sup>1</sup> is an aryl or heteroaryl group; and R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as defined in the claims. Also provided are pharmaceutical compositions containing the compounds, methods for preparing the compounds and their use as anticancer agents.

WO 2005/061463 A1



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.